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EXAMINER
FOSTER, CHRISTINE E

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pat-dept@quarles.com

Office Action Summary	Application No.	Applicant(s)	
	10/711,517	ABBOTT ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,11 and 14-41* is/are pending in the application.

4a) Of the above claim(s) *24-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10,11 and 14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *9/23/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment, filed 10/10/07, is acknowledged and has been entered. Claims 1-3, 6, and 14 have been amended. Claims 7-9 and 13 have been canceled. Accordingly, claims 1-6, 10-11, and 14-41 are pending in the application, with claims 1-6, 10-11, and 14-23 under examination.

Objections/Rejections Withdrawn

2. The objections to and rejections of claims 7-9 and 13 are moot in light of Applicant's cancellation of the claims.

3. The objections to claims 3, 6, 14, 18, and 21 have been obviated by the amendments thereto.

4. The rejections of claims 1-6, 10-11 and 14-23 under § 112, 1st paragraph have been withdrawn in response to Applicant's amendments to claim 1.

5. The rejections of claims 1-6, 10-11 and 14-23 under § 112, 2nd paragraph have been obviated by the claim amendments. However, the amended claims have presented new grounds of rejection under this statute as set forth below.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-6, 10-11, 15-20 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 1 as amended recites

> (c) detecting the presence of the ligand on the detection surface by contacting the detection surface with a liquid crystal, wherein the presence of the ligand on the detection surface is detected ***by a change in the orientation of the liquid crystal*** contacted with the detection surface.

(emphasis added)

The claim is indefinite because it is not clear what the change in liquid orientation is being assessed relative to. The claim previously recited that the detection surface already included a liquid crystal prior to application of the ligand. Therefore, reference to a "change" was meaningful in the context of before and after ligand binding to the detection surface. However, the claim now reads on methods in which the ligand is applied to the detection surface first and then the liquid crystal is subsequently applied to the surface. In this case, it is not clear what the change in orientation would be assessed relative to, since the liquid crystal would not yet be oriented or anchored on the surface before ligand binding. Therefore, it is not clear how a "change" in orientation would be assessed. Is the change relative to the orientation of liquid crystals on a control detection surface having no printed ligand? Or relative to other areas of the surface not contacted by the affinity substrate?

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-6, 10-11, 15-20 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Bernard et al. ("Affinity capture of proteins from solution and their dissociation by contact printing" (2001) *Nature Biotechnology* **19**:866-869) or alternatively over Renault et al. (*Agnew. Chem. Int. Ed.* 2002, 41, No. 13, 2320-2323, Applicant's IDS of 1/30/2006 and the Supporting Information for the article obtained from http://www.angewandte.org on 3/21/07) in view of Abbott et al. (US 6,284,197 B1, Applicant's IDS of 1/30/2006).

Bernard et al. teach a method for detecting a ligand comprising (a) contacting a sample having a ligand ("target molecule", for example ^{125}I-IgG) with an affinity substrate (polydimethylsiloxane (PDMS) stamp), wherein the affinity substrate comprises receptors ("capturing molecules") that are capable of specifically binding the ligand. The receptors are for example anti-mouse IgGs, which is capable of specifically binding to IgG. Bernard et al. also teach that the affinity substrate could be patterned with various different types of capturing

molecules in order to screen for several ligands in a parallel manner (see the paragraph bridging pages 868-869). See entire selection, in particular the abstract; Figures 1-2 and p. 866, left column and the paragraph bridging the left and right columns; and p. 869, "Derivatization of stamps".

Bernard et al. further teach (b) contacting the affinity substrate with a detection surface (glass or polystyrene), wherein at least a portion of the ligand that is bound to the receptor is transferred to the detection surface (see in particular p. 866, left column, second paragraph; p. 867, left column; Figure 3; the first paragraph of "Results and Discussion" on p. 866; and also p. 869, "Affinity stamping").

Bernard et al. differs from the claimed invention in that it fails to specifically teach detecting the presence of the ligand by contacting the detection surface with a liquid crystal, wherein a change in the orientation of the liquid crystal indicates the presence of a ligand. By contrast, in Bernard et al., the printed ligands are detected using radioactive or fluorescent labels attached to the target ligands (see especially p. 866, right column; p. 869, right column; and Figures 2 and 4).

Like Bernard et al., Renault et al. similarly teaches an affinity capture method followed by microcontact printing. In particular, Renault et al. teaches a method for detecting ligands ("target molecules", e.g. antibodies) by contacting a sample (e.g., solution containing target antibodies) with an affinity substrate (PDMS elastomeric stamp) (see entire selection, especially p. 2320, left column and the paragraph bridging the left and right columns; p. 2323, left column, last paragraph; and Figures 1, 2d, and 3-4). The affinity substrate comprises an array of receptors ("capture molecules") on the substrate, defining various capture sites that each have different

capture molecules capable of specifically binding to different target proteins (see depiction in Figure 1A; p. 2321, right column and also p. 2320, the paragraph bridging the left and right columns).

Renault et al. further teach contacting the affinity substrate with a detection surface ("substrate", which was glass in the examples); see also p. 2322, left column. This results in the captured target molecules being transferred onto the substrate (see depiction in Figure 1E).

However, like Bernard et al., the teachings of Renault et al. differ from the claimed invention in that the reference fails to specifically teach detecting the presence of the ligand by contacting the detection surface with a liquid crystal, wherein a change in the orientation of the liquid crystal indicates the presence of a ligand. As in Bernard et al., detection of the presence of the ligand on the detection surface was performed using labeled target molecules. Specifically, Renault et al. teach detection of fluorescent- or gold-labeled antibodies by fluorescence microscopy or atomic force microscopy, respectively (see especially Figure 5).

Abbott et al. teach devices and methods for detecting a ligand based on the use of liquid crystals to amplify and transduce into an optical signal the interaction of a wide array of molecules with various surfaces (see entire selection, in particular the abstract; column 4, line 49 to column 5, line 26).

To perform liquid crystal detection, the ligand is bound to the surface of the substrate, liquid crystal is contacted with the substrate in the form of a mesogenic layer, and the orientation of the liquid crystal is assessed. See in particular the abstract; column 32, lines 21-29; claim 1, step (b) in particular; column 30, line 29 to column 32, line 29; and Example 1. In other embodiments, the ligand may be bound to the surface of liquid crystal devices in which the

liquid crystal is already coupled to the surface (column 13, lines 4-25; and column 5, line 13 to column 6, line 14).

The liquid crystal (mesogens) undergo a detectable switch in orientation upon interaction of the ligand with the surface, allowing for the ligand to be detected (column 5, line 13 to column 6, line 3; column 13, lines 3-31; column 14, lines 15-43; column 20, lines 4-12; column 38, line 46 to column 39, line 50). Interaction-induced changes in the mesogenic layer can be easily seen with the naked eye (column 5, lines 18-27).

Abbott et al. teach that the use of liquid crystals in devices to detect allows for simple, inexpensive, and reliable detection and characterization of analytes (column 4, line 61 to column 5, line 10). Specifically, Abbott et al. teach that liquid crystal detection obviates the need for prelabeling of ligand, such as with a radiolabel or a fluorescent moiety (see column 5, lines 5-10).

Therefore, it would have been obvious to one of ordinary skill in the art to employ liquid crystal detection as taught by Abbott et al. (substrate comprising a liquid crystal) in place of fluorescent, gold, or radioactive labeling-based detection as the means of detecting the ligand in the methods of Bernard et al. or Renault et al. In particular, it would have been obvious to subsequently contact the ligand-printed detection surfaces of Bernard et al. or Renault et al. with a liquid crystal (e.g., in the form of an organic mesogenic layer) as taught by Abbott et al. and to detect the presence of the ligand on the surface via a change in the liquid crystal orientation. One would have a reasonable expectation of success because the detection surfaces taught by Renault et al. and Bernard et al. (glass and/or polystyrene) are taught by Abbott et al. as suitable substrates for liquid crystal detection (see Abbott et al. at columns 14-15).

In addition, since claim 1 does not require a particular order in which the liquid crystal is contacted with the liquid crystal (as recited in step (c)) this means that the detection surface could be contacted with the liquid crystal prior to application of the ligand. Therefore, it would also have been obvious to arrive at the claimed invention by employing the liquid crystal devices of Abbott et al. (having liquid crystal already coupled to the substrate surface) as the detection surface on which the ligand is microcontact printed and to detect the ligand by a change in orientation of the liquid crystal in the methods for detecting a ligand of either Bernard et al. or Renault et al. One would also have a reasonable expectation of success in affinity stamping the surface of Abbott et al. according to the method of Bernard et al. or Renault et al. because the surface of Abbott et al. is compatible with microcontact printing (see column 17, lines 5-22).

One would be motivated to combine the reference teachings as discussed above because Abbott et al. teach that liquid crystal detection surfaces do not require prelabeling of the ligand (as was performed in Bernard et al. and Renault et al.). As such, one would be motivated to stamp the affinity-captured ligand onto the device of Abbott et al. in order to avoid the need for using fluorescent or other labels on the ligands.

With regard to claim 2, Bernard et al. teach (a) washing the affinity substrate after the contacting step (a) above (p. 869, "Affinity stamping"). Renault et al. also teach (a) rinsing the stamp after contacting it with the sample (see especially the legend to Figure 2).

With regard to claims 4-5, Bernard et al. teach affinity substrates consisting of PDMS as an inert elastomer (p. 866, left column, paragraph 3). Renault et al. also teaches a PDMS elastomeric stamp (see especially p. 2320, left column).

With respect to claim 6, the PDMS affinity substrates of Bernard et al. are "antibody-terminated" in that the antibodies are attached to the ends of PDMS stamps (Figure 1). The antibodies are capable of binding to a protein (^{125}I-IgG). Bernard et al. teach the use of antibodies in this context as capturing molecules (e.g., see p. 866, first two paragraphs of "Results and Discussion"). Similarly, Renault et al. teach attaching the capture molecules (which may be antibodies) to the surface or end of the PDMS stamps (Figure 1 and p. 2320-2321).

With regard to claim 10, Bernard et al. teach that the antibodies, protein A, and streptavidin were applied to the affinity stamps via the cross-linker BS3 (p. 869, "Derivatization of stamps"). Renault et al. similarly teach that the receptors are attached via this same crosslinker (p. 2320, right column).

With regard to claim 11, while not specifically recited by Bernard et al., the amount of ligand present in the sample was necessarily quantified because Bernard et al. teach the concentrations of the ligands TRITC-labeled rabbit IgG and biotinylated alkaline phosphatase in the samples (see p 869, "Affinity Stamping and Figure 2A). Similarly, Renault et al. report the quantity of the ligand in the sample (see Supporting Information, page 1), such that the ligand was necessarily quantified.

With regard to claims 15-17 and 19, Abbott et al. further teach that the detection surface may comprise self-assembled monolayers in order to anchor the liquid crystal mesogenic layer, where the self-assembled monolayers may be formed from alkanethiols or organosulfur compounds and may comprise amines through functionalization (the abstract; column 19, line 25 to column 21, line 16). Abbott et al. teach that use of certain self-assembled monolayers enables homeotropically anchoring of mesogens, and that homeotropic anchoring is the most preferred

anchoring direction (see especially column 18, line 4, to column 19, line 45). Abbott et al. teach that the detection surface may be treated with 1-aminododecanoic acid to make the surface surface-active (column 25, lines 26-31).

With regard to claim 18, the specification discloses that "The method comprises the steps of: (a) contacting the ligand to a first surface, wherein the ligand is at least in part attached to the first surface; (b) contacting the ligand-decorated first surface to a second surface, wherein the ligand is at least in part attached to the second surface, *such that at least a portion of the first surface is partially curved*" (paragraph 28, emphasis added). Thus, the specification indicates that partial curvature of the affinity substrate occurs as a result of contacting the affinity substrate with a surface. In the absence of any specific structural limitations recited, the methods of Bernard et al. or Renault et al. and Abbott et al. meet the claim since in the course of contacting the affinity substrates of Bernard et al. or Renault et al. with the detection surface of Abbott et al., the surface of the affinity substrates would become partially curved as indicated by the specification.

With regard to claims 20 and 22, the liquid crystal mesogens of Abbott et al. may be thermotropic or lyotropic and may be nematic, chiral nematic, smectic, frustrated liquid crystals, or discotic liquid crystals (column 30, line 30 to column 32, line 29), and a preferred liquid crystal is 4-cyano-4'-pentylbiphenyl (5CB) (column 37, lines 53-59).

With regard to claim 23, Abbott et al. teach that the detection surface allows for optical detection of orientation of the liquid crystal (mesogens), which allows for ease of detection (column 5, lines 13-26). Electrical detection may also be employed (column 38, lines 56-63).

12. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. or Renault et al. in view of Abbott et al. as applied to claim 1 above, and further in view of Tang et al. (US Patent No. 5,886,195).

Bernard et al., Renault et al., and Abbott et al. are as discussed above, which fail to specifically teach a method wherein the receptor is capable of detecting the presence of protein phosphorylation in EGFR residues.

Tang et al. teach anti-phosphotyrosine antibodies, which may be used to measure autophosphorylation of EGFR and thereby an increase in EGF activity (column 6, lines 53-65).

Therefore, it would have been obvious to one of ordinary skill in the art to employ anti-phosphotyrosine antibodies as taught by Tang et al. as the capturing molecule on the PDMS affinity substrates in the method for detecting a ligand of Bernard et al. and Abbott et al., or alternatively of Renault et al. and Abbott et al., in order to measure autophosphorylation of EGFR residues. One would have reasonable expectation of success because Bernard et al. and Renault et al. teach that antibodies can be used as capture molecules on PDMS stamps.

13. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. or Renault et al. in view of Abbott et al. as applied to claim 1 above, and further in view of Choi et al. (US 6,292,296).

Bernard et al., Renault et al., and Abbott et al. are as discussed above, which fail to treat a method wherein the liquid crystal is pretreated by illumination with UV light.

Choi et al. teach methods for aligning liquid crystal devices, including rubbing as well as photo-alignment using ultraviolet light (column 1, lines 10-51). The reference teaches that

compared with the rubbing method, there is no electrostatic discharge or dust particles associated with photo-alignment, thus obviating low yield problems.

Therefore, would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the liquid crystal detection surface of Abbott et al. by photo-alignment with ultraviolet light as taught by Choi et al. (rather than by rubbing as exemplified by Abbott et al.), in the method of Bernard et al. (or Renault et al.) and Abbott et al. order to align the liquid crystal detection surface while avoiding disadvantages such as dust particles that are known to be associated with the rubbing method.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-6, 10-11, and 14-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18-23 of copending Application No. 11/542,432 in view of Renault et al.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the '432 application also claims a method for detecting a ligand (analyte) in which an affinity substrate ("affinity stamp") is used to transfer a captured analyte from the stamp to a detection surface ("substrate surface") by microcontact printing (see especially claims 18-19). Although the '432 application fails to specifically recite that the affinity substrate is contacted with a sample having or suspected of having the ligand, such a step would be immediately envisaged since the claims recite a method of detecting an analyte *in a sample*. The '432 application further recites the step of detecting the presence of the ligand by introducing a liquid crystal to the detection surface and detecting a change or departure in the orientation of the liquid crystal (see especially claim 18, steps (b)-(c) and claims 22-23).

The '432 application differs from the claimed invention in that it fails to specifically recite that the affinity substrate comprises an array of receptors, wherein each receptor is capable of specifically binding to a ligand.

However, Renault et al. teaches methods of transferring captured analytes from affinity stamps by affinity microcontact printing. The reference teaches assembling an "array" of various types of capturing molecules on the surface of a stamp (see especially Figure 1 and p. 2320, the paragraph bridging the left and right columns). The reference teaches that this allows simultaneous capture of different target proteins from a complex solution (ibid).

Therefore, it would have been obvious to one of ordinary skill in the art to provide the affinity stamp of the '432 application with an array of receptors in order to enable simultaneous capture of different target proteins from a complex solution.

16. Claims 1-6, 10-11, and 14-23 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-34 of copending Application No. 11/418,755 in view of Renault et al.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the '755 application also claims a method for detecting the presence of an analyte in a sample suspected of containing the analyte by exposing the sample with an affinity substrate (stamp comprising a pad functionalized with a ligand) and then contacting the affinity substrate with a detection surface ("detection region") (see especially claim 21). The presence of the analyte on the detection region is determined by contacting the detection surface with a mesogen to form a liquid crystal and detecting a change in the orientation ("ordering") of a liquid crystal (see step (6) of claim 21 and also claim 34).

The '755 application differs from the claimed invention in that it fails to specifically recite that the affinity substrate comprises an array of receptors, wherein each receptor is capable of specifically binding to a ligand.

However, Renault et al. teaches methods of transferring captured analytes from affinity stamps by affinity microcontact printing. The reference teaches assembling an "array" of various types of capturing molecules on the surface of a stamp (see especially Figure 1 and p. 2320, the paragraph bridging the left and right columns). The reference teaches that this allows simultaneous capture of different target proteins from a complex solution (ibid).

Therefore, it would have been obvious to one of ordinary skill in the art to provide the affinity stamp of the '432 application with an array of receptors in order to enable simultaneous capture of different target proteins from a complex solution.

The above are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Response to Arguments

17. Applicant's arguments filed 10/10/2007 have been fully considered.

18. With respect to the rejections of claims 1-6, 10-11, 15-20 and 22-23 under § 103 as being unpatentable over Bernard et al. or, alternatively, over Renault et al. in view of Abbott et al., Applicant's arguments (see pages 10-15 of the Reply) have been fully considered but are not persuasive of error.

Applicant argues that there is a lack of teachings/guidance provided in the cited references and in the general knowledge in the art at the time of the invention, as well as a lack of expectation of success and predictability (Reply, page 11, the first full paragraph). In particular, Applicant argues that the primary references (Bernard et al. and Renault et al.) do not teach liquid crystal detection (Reply, page 11, the last paragraph to page 12, the first full paragraph; and also page 13, the first full paragraph).

This is not found persuasive since it amounts to a piecemeal analysis of the references. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re*

Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the Office has not contended that the primary references teach liquid crystal detection; rather, the Abbott et al. reference has been relied on for this teaching.

Applicant further argues that the secondary reference (Abbott et al.) does not teach affinity microcontact printed ligands (Reply, page 13, the second full paragraph), which is not found persuasive since as above, such arguments amount to a piecemeal analysis of the references; the indicated teaching is found in the primary references.

Applicant further argues that the discussion of microcontact printing in the Abbott et al. reference was not in regards to "affinity" microcontact printing, and has submitted a Declaration by Dr. Abbott to this effect. The Declaration under 37 CFR 1.132 filed 10/10/07 is insufficient to overcome the rejection of claims 1-6, 10-11, 15-20 and 22-23 under § 103 based upon Bernard et al. or, alternatively, over Renault et al. in view of Abbott et al., as set forth in the last Office action because:

The Declaration, as well as Applicant's arguments in the Reply on page 13, the last paragraph to page 14, the second paragraph, have apparently been advanced to establish the point that microcontact printing was disclosed by Abbott et al. in a different context, namely in the context of fabricating the detection surface prior to detection.

However, the Office has not contended that Abbott et al. teach combining microcontact printing with liquid crystal detection in the manner claimed by Applicant. It is acknowledged that the teaching of microcontact printing by Abbott et al. is in a different context. No contention to the contrary is made in the rejection. Rather, the Examiner has pointed to this teaching because it indicates that the detection substrates of Abbott et al. can be subjected to microcontact

printing, which adds further evidence that one of ordinary skill in the art would have a reasonable expectation of success in combining the liquid crystal detection methods of Abbott et al. with the affinity microcontact printing methods of Bernard et al. or Renault et al.

Therefore, Applicant's arguments that the disclosure of microcontact printing in Abbott et al. is in a different context are seen as tangential to the instant rejection because they represent an attempt to rebut a position that has not been taken by the Office.

Applicant further points to a lack of predictability in combining the prior known elements (see, e.g., page 11, first full paragraph) but has not sufficiently documented or explained such unpredictability. For example, Applicant has not pointed to any specific technical obstacles overcome by the instant invention. The Arguments of counsel cannot take the place of factually supported objective evidence.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

19. With respect to the provisional nonstatutory obviousness-type double patenting rejections, Applicant has acknowledged the rejections but does not present arguments traversing the rejections at this time (Reply, pages 15-16).

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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